3-8-07

Express Mail Label No.: EV978769507US
Date of Deposit: March 6, 2007

Attorney Docket No. 24024-506CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Peled *et al.*
SERIAL NUMBER : 10/767,064 EXAMINER : Singh, Anoop Kumar
FILING DATE : January 29, 2004 ART UNIT : 1632
FOR : EX-VIVO EXPANSION OF HEMATOPHOIETIC STEM CELL POPULATIONS IN MONONUCLEAR CELL CULTURES

Office of Initial Patent Examination's
Filing Receipt Corrections
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Transmitted herewith for filing in the above-referenced patent application are the following documents:

1. Communication (2 pgs);
2. Request for Corrected Filing Receipt (2 pgs.);
3. Copy of Filing Receipt Marked with Corrections (2 pgs.);
4. Copy of Request for Continuation Application and Preliminary Amendment (14 pgs);
5. Copy of Response to Request for Corrected Filing Receipt (2 pgs); and
4. Return postcard.

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at 617-542-6000, Boston, Massachusetts.

The Commissioner is authorized to charge any fees that may be due to the undersigned's account, Deposit Account No. 50-0311, Ref. No. 24024-506 CON. A duplicate copy of this transmittal letter is enclosed herewith.

Respectfully submitted,

Ivor R. Elrifi, Reg. No. 39,529
Matthew Pavao, Reg. No. 50,572
Attorneys for Applicants
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623

Dated: March 6, 2007

3985496v.1

Express Mail Label No.: EV978769507US
Date of Deposit: March 6, 2007

Attorney Docket No. 24024-506CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Peled *et al.*

SERIAL NUMBER : 10/767,064 EXAMINER : Singh, Anoop Kumar

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Office of Initial Patent Examination's
Filing Receipt Corrections
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

COMMUNICATION

This communication is further to the Request for Corrected Filing Receipt filed on January 28, 2005 in above-identified application. It appears that no action was taken by the Office of Initial Patent Examination as Applicants did not receive an updated filing receipt in response to the January 28, 2005 Request. As such, Applicants herewith reiterate a Request for Corrected Filing Receipt.

The Response to Request for Corrected Filing Receipt mailed January 13, 2005 indicates that the applications to which priority is claimed (60/404,137 and 60/404,145) were filed over a year prior to the filing date of this application (10/767,064). Therefore, the referenced applications (60/404,137 and 60/404,145) cannot be claimed as domestic or foreign priority. Applicants disagree.

The instant application is a continuation application and claims the benefit of, and priority to, PCT/IL03/00681, filed August 17, 2003, under 35 USC § 365(c). PCT/IL03/00681, filed August 17, 2003, properly claims the benefit of, and priority to, the following applications:

PCT/IL03/00064 filed January 26, 2003;

PCT/IL03/00062 filed January 23, 2003;

Israel Patent Application IL152904 filed November 17, 2002;

U.S. Patent Application 60/404,137 filed August 19, 2002;

U.S. Patent Application 60/452,545 filed March 7, 2003; and

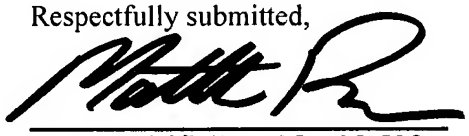
U.S. Patent Application 60/404,145 filed August 19, 2002.

As the instant application is a continuation application of PCT/IL03/00681, filed August 17, 2003, which properly claims the benefit of, and priority to, U.S. Patent Application 60/404,137, filed August 19, 2002 and U.S. Patent Application 60/404,145, filed August 19, 2002, Applicants submit the instant application is entitled to claim priority to these applications.

Applicants believe that no fees are due with this filing. However, the Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment, to Deposit Account No. 50-0311, Attorney Ref. No. 24024-506 CON.

If there are any questions regarding these references, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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Dated: March 6, 2007

Express Mail Label No.: EV978769507US
Date of Deposit: March 6, 2007

Attorney Docket No. 24024-506CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Peled *et al.*
SERIAL NUMBER : 10/767,064 EXAMINER : Sing, Snoop Kumar
FILING DATE : January 29, 2004 ART UNIT : 1632
FOR : EX-VIVO EXPANSION OF HEMATOPHOIETIC STEM CELL POPULATIONS IN MONONUCLEAR CELL CULTURES

Office of Initial Patent Examination's
Filing Receipt Corrections
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CORRECTED FILING RECEIPT

1. Applicants request a Corrected Filing Receipt for the above-mentioned patent application. Applicants enclose a copy of the Filing Receipt with the corrections noted thereon. Issuance of a corrected filing receipt is respectfully requested.

2. There are errors with respect to the following data, which are:

☒ incorrectly entered

and/or

☐ omitted.

	Error in	*Correct data*
1. ☐	Applicants' name	
2. ☐	Applicants' address	
3. ☐	Title	
4. ☐	Filing Date	
5. ☐	Serial Number	
6. ☒	Domestic Priority Data	This application claims the benefit of 60/452,545 filed 03/07/2003 60/404,137 filed 08/19/2002 60/404,145 filed 08/19/2002
7. ☒	Foreign Applications	ISRAEL 152904 filed 11/17/2002 PCT/IL03/00681 filed 08/17/2003 PCT/IL03/00064 filed 01/26/2003

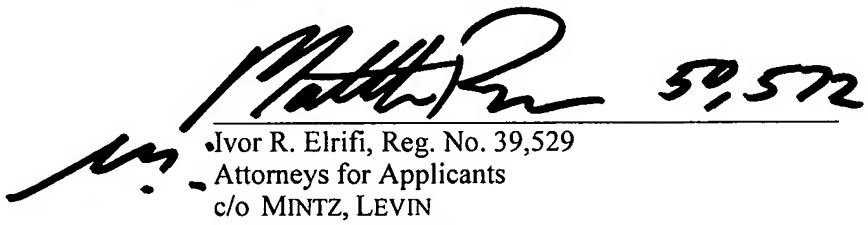
Error in	*Correct data*
8. ☐ Other	PCT/IL03/00062 filed 01/23/2003

4. Applicants herewith include a Response to the January 13, 2005 Response to Request for Corrected Filing Receipt describing the priority for the instant application.

5. Applicants submit that the priority information was included with Applicant's Request for Filing a Continuation Patent Application under 37 CFR 1.53(b) and the Preliminary Amendment filed therewith on January 29, 2004.

6. Applicants believe that no fee is due. However, the Commissioner is authorized to charge any fees that may be due, or to credit any overpayment, to Deposit Account No. 50-0311, Ref. No. 24024-506CON.

Respectfully submitted,



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Dated: March 6, 2007

3985502v.1

Exp# EV978769507US
Date of Dep: 3/6/07

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY.DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/767,064	01/29/2004	1642	872	24024-506	2	43	8

CONFIRMATION NO. 5661

30623
MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

CORRECTED FILING RECEIPT

OC000000014957443

Date Mailed: 01/13/2005

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Tony Peled, Mevaseret Zion, ISRAEL;
Avi Treves, Mevaseret Zion, ISRAEL;
Oren Rosen, Jerusalem, ISRAEL;

Power of Attorney: The patent practitioners associated with Customer Number **30623**.

Domestic Priority data as claimed by applicant

This appln claims benefit of 60/452,545 03/07/2003, 60/404,137 Filed 8-19-02 and 60/404,145 Filed 8-19-02.

Foreign Applications

ISRAEL 152904 11/17/2002
ISRAEL PCT/IL03/00681 08/17/2003
ISRAEL PCT/IL03/00064 01/26/2003
ISRAEL PCT/IL03/00062 01/23/2003

If Required, Foreign Filing License Granted: 06/14/2004

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is US10/767,064

Projected Publication Date: 03/10/2005

Non-Publication Request: No

Early Publication Request: No

** SMALL ENTITY **

Title

EX-VIVO expansion of hematopoietic system cell populations in mononuclear cell cultures

Preliminary Class

435

LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10 (j)); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

Express Mail Label No.: EV 703020US
Date of Deposit: January 29, 2004

Attorney Docket No. 24024-506 (GE26736)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FIRST-NAMED INVENTOR: Tony Peled

FOR: *EX-VIVO* EXPANSION OF HEMATOPOIETIC STEM CELL POPULATIONS IN MONONUCLEAR CELL CULTURES

Mail Stop PATENT APPLICATION
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR FILING A CONTINUATION PATENT APPLICATION UNDER 37 C.F.R. §1.53(b)

1. This is a request for filing a 35 USC§ 111(a) continuation application. This continuation application claims the benefit of, and priority to, under 35 USC § 365(c) to PCT/IL03/00681, filed August 17, 2003, which claims priority from PCT/IL03/00064 filed January 26, 2003 which claims priority from Israel Patent Application IL152904 filed November 17, 2002 and U.S. Patent Application 60/404,137 filed August 19, 2002, now abandoned; PCT/IL03/00062 filed January 23, 2003; U.S. Patent Application 60/452,545 filed March 7, 2003 and U.S. Patent Application 60/404,145 filed August 19, 2002, now abandoned. This continuation application also claims priority to each of these provisional patent applications. The contents of all of these referenced applications are incorporated herein by reference in their entireties.

2. A true copy of the parent application PCT/IL03/00681 is enclosed. This application is a total of 160 pages. This application includes:

   97 pages of specification (not including claims, abstract, or figures)
   62 pages of claims
   1 page of abstract
   2 sheets of drawings (Figs. 1A-3)

3. An unsigned copy of the Combined Declaration/Power of Attorney is enclosed (3 pgs).

4. Please enter the accompanying Preliminary Amendment prior to calculating the fees due for this filing. Fees associated with this application are calculated as follows.

CLAIMS AS FILED					
Claims	Number Filed	Basic Fee Allowance	Number Extra	Rate	Basic Fee 37 C.F.R. 1.16(a) $770.00
Total Claims (37 C.F.R. 1.16(c))	43	– 20 =	23	$18.00	$414.00
Independent Claims (37 C.F.R. 1.16(b))	8	– 3 =	5	$86.00	$430.00
Multiple Dependent Claim(s), if any (37 C.F.R. 1.16(d))	-0-			$270.00	
				SUBTOTAL:	$1,614.00
			Reduction by 50% for filing by small entity:		**$807.00**
				TOTAL FEE:	**$807.00**

5. A check (#17986) in the amount of **$807.00** is enclosed. The Commissioner is authorized to charge any additional fees due, or credit overpayments, to Deposit Account No. 50-0311, Ref. No. 24024-506.

6. A return receipt postcard is enclosed.

Respectfully submitted,

Ivor R. Elrifi, Reg. No. 39,529
David E. Johnson, Reg. No. 41,874
Attorney for Applicants
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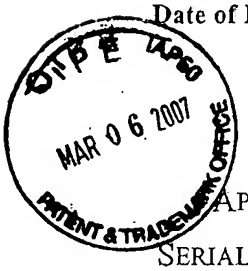
Customer No. 30623

Dated: January 29, 2004

TRA 1879959v1

Express Mail Label No.: EV 703020US
Date of Deposit: January 29, 2004

Attorney Doc. 24024-506 (GE No. 26736)



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Peled et al.		
SERIAL NUMBER:	Not Yet Assigned	EXAMINER:	Not Yet Assigned
FILING DATE:	Not Yet Assigned	ART UNIT:	Not Yet Assigned

FOR: EX VIVO EXPANSION OF HEMATOPOIETIC STEM CELL POPULATIONS IN MONONUCLEAR CELL CULTURES

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Preliminary Amendment

Prior to examination, please amend the application as follows.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims, which begins on page 3 of this paper.

Remarks begin on page 12 of this paper.

Amendments to the Specification:

Following the title on page 1, please add the following section:

RELATED APPLICATIONS

This application is a 35 U.S.C. §111 continuation application claiming the benefit of, and priority to, under 35 USC § 365(c) to PCT/IL03/00681, filed August 17, 2003, which claims priority from PCT/IL03/00064 filed January 26, 2003 which claims priority from Israel Patent Application IL152904 filed November 17, 2002 and U.S. Patent Application 60/404,137 filed August 19, 2002, now abandoned; PCT/IL03/00062 filed January 23, 2003; U.S. Patent Application 60/452,545 filed March 7, 2003 and U.S. Patent Application 60/404,145 filed August 19, 2002, now abandoned. The contents of all of these priority applications are incorporated herein by reference in their entireties.

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-200 (cancelled).

201. (new) A method of expanding an *ex-vivo* population of hematopoietic stem cells, while at the same time, substantially inhibiting differentiation of the hematopoietic stem cells *ex-vivo*, the method comprising

providing hematopoietic mononuclear cells;

culturing said mononuclear cells *ex-vivo* under conditions allowing for cell proliferation and, at the same time, culturing said cells under conditions selected from the group consisting of

conditions reducing expression and/or activity of CD38 in said mononuclear cells,

conditions reducing capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoids and/or Vitamin D in said mononuclear cells,

conditions reducing capacity of said hematopoietic mononuclear cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said mononuclear cells;

culturing said mononuclear cells in the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite in said mononuclear cells;

conditions reducing an expression and/or activity of PI 3-kinase in said mononuclear cells; and

culturing said mononuclear cells in the presence of at least one copper chelator or chelate,

thereby expanding a population of said hematopoietic stem cells while at the same time substantially inhibiting differentiation of said hematopoietic stem cells *ex-vivo*.

202. (new) A method of transplanting or implanting hematopoietic cells, the method comprising:

(a) obtaining hematopoietic mononuclear cells;

(b) culturing said mononuclear cells ex vivo for cell proliferation, wherein said culturing is performed in a condition selected from the group consisting of

~~reducing expression and/or activity of CD38,~~

reducing a capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoids and/or Vitamin D,

reducing capacity of said hematopoietic mononuclear cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor;

the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite;

reducing an expression and/or activity of PI 3-kinase or

the presence of at least one copper chelator or chelate,

thereby expanding a population of said hematopoietic stem cells, while at the same time, substantially inhibiting differentiation of said hematopoietic stem cells *ex-vivo*; and

(c) transplanting or implanting said hematopoietic stem cells to a recipient.

203. (new)The method of claim 202, wherein said donor and said recipient are a single individual.

204. (new) A method of genetically modifying hematopoietic stem cells with an exogene comprising:

(a) obtaining hematopoietic mononuclear cells;

(b) culturing said mononuclear cells ex vivo for cell proliferation, wherein said culturing is performed in a condition selected from the group consisting of

conditions reducing expression and/or activity of CD38 in said mononuclear cells,

conditions reducing capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoids and/or Vitamin D in said mononuclear cells,

conditions reducing capacity of said hematopoietic mononuclear cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said mononuclear cells;

culturing said mononuclear cells in the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite in said mononuclear cells;

conditions reducing an expression and/or activity of PI 3-kinase in said mononuclear cells; and

culturing said mononuclear cells in the presence of at least one copper chelator or chelate,

thereby expanding a population of said hematopoietic stem cells, while at the same time, substantially inhibiting differentiation of said hematopoietic stem cells *ex-vivo*; and

(c) genetically modifying said hematopoietic stem cells with the exogene.

205. (new) The method of claim 204, wherein genetically modifying is effected by a vector which comprises the exogene.

206. (new) The method of claim 205, wherein the vector is a viral vector or a nucleic acid vector.

207. (new) A method of adoptive immunotherapy comprising:

(a) obtaining hematopoietic mononuclear cells from a recipient;

(b) culturing said mononuclear cells ex vivo for cell proliferation, wherein said culturing is performed in a condition selected from the group consisting of

conditions reducing expression and/or activity of CD38 in said mononuclear cells,

conditions reducing capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoids and/or Vitamin D in said mononuclear cells,

conditions reducing capacity of said hematopoietic mononuclear cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said mononuclear cells;

culturing said mononuclear cells in the presence of nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite in said mononuclear cells;

conditions reducing an expression and/or activity of PI 3-kinase in said mononuclear cells; and

culturing said mononuclear cells in the presence of at least one copper chelator or chelate,

thereby expanding a population of said hematopoietic stem cells, while at the same time, substantially inhibiting differentiation of said hematopoietic stem cells; and

(c) transplanting said hematopoietic stem cells to the recipient.

208. (new) A transplantable hematopoietic cell preparation comprising an expanded population of hematopoietic stem cells propagated *ex-vivo* from hematopoietic mononuclear cells in the presence of an effective amount of an agent,

wherein said agent has an activity selected from the group consisting of

reducing expression and/or activity of CD38 in said mononuclear cells,

reducing capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoids and/or Vitamin D in said mononuclear cells,

reducing capacity of said hematopoietic mononuclear cells in responding to signaling pathways involving the retinoic acid receptor, the retinoid X receptor and/or the Vitamin D receptor in said mononuclear cells; and

reducing an expression and/or activity of PI 3-kinase in said mononuclear cells; or wherein said agent is

a copper chelator or chelate, or

nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite in said mononuclear cells;

while at the same time, substantially inhibiting differentiation of said hematopoietic stem cells, and a pharmaceutically acceptable carrier.

209. (new) The method of claim 201, wherein said hematopoietic mononuclear cells are derived from a source selected from the group consisting of bone marrow, peripheral blood and neonatal umbilical cord blood.

210. (new) The method of claim 201, wherein providing said hematopoietic mononuclear cells with said conditions for *ex-vivo* cell proliferation comprises providing said hematopoietic mononuclear cells with nutrients and with cytokines.

211. (new) The method of claim 210, wherein said cytokines are early acting cytokines.

212. (new) The method of claim 211, wherein said early acting cytokines are selected from the group consisting of stem cell factor, FLT3 ligand, interleukin-1, interleukin-2, interleukin-3, interleukin-6, interleukin-10, interleukin-12, tumor necrosis factor-a and thrombopoietin.

213. (new) The method of claim 210, wherein said cytokines are late acting cytokines.

214. (new) The method of claim 213, wherein said late acting cytokines are selected from the group consisting of granulocyte colony stimulating factor, granulocyte/macrophage colony stimulating factor, erythropoietin, FGF, EGF, NGF, VEGF, LIF, Hepatocyte growth factor and macrophage colony stimulating factor.

215. (new) The method of claim 201, wherein providing said hematopoietic mononuclear cells with *ex-vivo* culture conditions for reducing said expression and/or said activity of CD38 is by providing said hematopoietic mononuclear cells with an agent that downregulates CD38 expression.

216. (new) The transplantable hematopoietic cell preparation of claim 208, wherein said agent is an agent that downregulates CD38 expression.

217. (new) The method of claim 215, wherein the agent that downregulates CD38 expression is selected from the group consisting of a retinoic acid receptor antagonist, a retinoid X receptor antagonist and a Vitamin D receptor antagonist.

218. (new) The method of claim 215, wherein the agent that downregulates CD38 expression is an antagonist for reducing a capacity of said hematopoietic mononuclear cells in responding to retinoic acid, retinoid and/or Vitamin D.

219. (new) The method of claim 215, wherein said agent that downregulates CD38 expression is a polynucleotide.

220. (new) The method of claim 219, wherein the polynucleotide encodes an anti CD38, an anti retinoic acid receptor, an anti retinoid X receptor or an anti Vitamin D receptor intracellular antibody.

221. (new) The method of claim 219, wherein the polynucleotide encodes an anti CD38, an anti retinoic acid receptor, an anti retinoid X receptor or an anti Vitamin D receptor antibody.

222. (new) The method of claim 219, wherein said polynucleotide is a small interfering polynucleotide molecule directed to cause intracellular CD38, retinoic acid receptor, retinoid X receptor or Vitamin D receptor mRNA degradation.

223. (new) The method of claim 222, wherein said small interfering polynucleotide molecule is selected from the group consisting of an RNAi molecule, an anti-sense molecule, a rybozyme molecule and a DNAzyme molecule.

224. (new) The method of claim 215, wherein said agent that downregulates CD38 expression is an agent that downregulates PI 3-kinase expression.

225. (new) The method of claim 224, wherein said agent that downregulates PI 3-kinase expression is a polynucleotide.

226. (new) The method of claim 224, wherein agent that downregulates PI 3-kinase expression is an intracellular antibody.

227. (new) The method of claim 225, wherein said polynucleotide is a small interfering polynucleotide molecule directed to cause intracellular PI 3-kinase mRNA or gene degradation.

228. (new) The method of claim 227, wherein said small interfering polynucleotide molecule is selected from the group consisting of an RNAi molecule, an anti-sense molecule, a rybozyme molecule and a DNAzyme molecule.

229. (new) The method of claim 215, wherein said agent that downregulates CD38 expression is an agent that inhibits PI 3-kinase activity.

230. (new) The method of claim 229, wherein said agent that inhibits PI 3-kinase activity is selected from the group consisting of wortmannin and LY294002

231. (new) The method of claim 201, wherein providing said hematopoietic mononuclear cells with *ex-vivo* culture conditions for reducing said expression and/or said activity of CD38 is by providing said hematopoietic mononuclear cells with an agent that inhibits CD38 activity.

232. (new) The transplantable hematopoietic cell preparation of claim 208, wherein said agent is an agent that inhibits CD38 activity.

233. (new) The method of claim 232, wherein said agent that inhibits CD38 activity is nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite.

234. (new) The method of claim 233, wherein said nicotinamide analog is selected from the group consisting of benzamide, nicotinethioamide, nicotinic acid and α-amino-3-indolepropionic acid.

235. (new) The method of claim 201, wherein providing said hematopoietic mononuclear cells with *ex-vivo* culture conditions for reducing said expression and/or said activity of CD38 is by providing said hematopoietic mononuclear cells with an agent that inhibits PI 3-kinase activity.

236. (new) The transplantable hematopoietic cell preparation of claim 208, wherein said agent is an agent that inhibits PI 3-kinase activity.

237. (new) The method of claim 236, wherein said agent that inhibits PI 3-kinase activity is selected from the group consisting of wortmannin and LY294002.

238. (new) The method of claim 201, wherein said hematopoietic mononuclear cells are not enriched prior to culturing *ex-vivo* under conditions allowing for cell proliferation.

239. (new) The method of claim 201, wherein said hematopoietic cells comprise a major fraction of hematopoietic committed cells and a minor fraction of hematopoietic stem and progenitor cells.

240. (new) An assay for determining whether a transition metal chelate or chelator causes substantial inhibition or induction of differentiation of hematopoietic stem cells, the assay comprising:

culturing hematopoietic mononuclear cells in the presence of the transition metal chelate or chelator and monitoring differentiation of said hematopoietic stem cells, wherein if differentiation is increased as is compared to non-treated hematopoietic mononuclear cells, said transition metal chelate induces differentiation, whereas if differentiation is decreased as is compared to non-treated hematopoietic mononuclear cells, or if differentiation is absent altogether, said transition metal chelate inhibits differentiation.

241. (new) An assay for identifying an effective hematopoietic stem cell expansion agent, the assay comprising culturing hematopoietic mononuclear cells in the presence of a compound selected from the group consisting of

a retinoic acid receptor antagonist;

retinoid X receptor antagonist;

vitamin D receptor antagonist;

agent that inhibits PI 3-kinase activity; and

a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite,

and monitoring expansion of said hematopoietic stem cells, wherein if increased expansion and decreased differentiation of said hematopoietic stem cells occurs, as compared to non-treated hematopoietic mononuclear cells, the compound is an effective hematopoietic stem cell expansion agent.

242. (new) A hematopoietic stem cells collection/culturing bag supplemented with an effective amount of a compound selected from the group consisting of

a retinoic acid receptor antagonist, a retinoid X receptor antagonist and/or a Vitamin D receptor antagonist,

nicotinamide, a nicotinamide analog, a nicotinamide or a nicotinamide analog derivative or a nicotinamide or a nicotinamide analog metabolite; or

an agent that inhibits PI 3-kinase activity,

which substantially inhibits cell differentiation of a hematopoietic stem cells fraction of hematopoietic mononuclear cells.

243. (new) An *ex-vivo* expanded population of hematopoietic stem cells, obtained by the method of claim 1.

Remarks

Upon entry of the amendment, claims 201-243 will be pending in the application. Claims 1-200 are cancelled and claims 201-243 are added. Support for the new claims appears in original claims 1-200 as filed and, for new claims 238 and 239, at page 34, lines 27-30 (disclosing using hematopoietic mononuclear cells as a direct source for obtaining expanded population of hematopoietic stem cells with stem cell enrichment prior to expansion). No new matter is added.

Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding this amendment and/or these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below. The Commissioner is authorized to charge any fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Reference No. 24024-506.

Respectfully submitted,

Dated: January 29, 2004

FOR Ivor R. Elrifi, Reg. No. 39,529 Reg. No. 41,874

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APPLICATION NUMBER	FILING OR 371(c) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
10/767,064	01/29/2004	Tony Peled	24024-506

CONFIRMATION NO. 5661

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OC000000014957462

Date Mailed: 01/13/2005

RESPONSE TO REQUEST FOR CORRECTED FILING RECEIPT

Domestic Continuity and Foreign Priority

In response to your request for a corrected Filing Receipt, the Office is unable to comply with the request because:

- ☐ The priority or continuity claim has not been entered because it was not filed during the required time period. Applicant may wish to consider filing a petition to accept an unintentionally delayed claim for priority. See 37 CFR 1.55 or 1.78.
- ☐ Continuity claimed under 35 U.S.C. § 120 cannot be added to the Filing Receipt without the applicant supplying the relationship (continuation, divisional, or continuation-in-part) in an Application Data Sheet or amendment to the first page of the specification.
- ☐ A claim for priority cannot be made based on an application filed after the application making the claim.
- ☐ Domestic benefit and foreign priority claims will not be captured in a provisional application. A provisional application is not entitled to a right of priority or to the benefit of an earlier filing date of any other application. See 35 U.S.C. § 111(b)(7) and 37 CFR 1.53(c)(4).
- ☐ A domestic continuity claim cannot be made to a foreign application and the filing receipt will only list the foreign country, application number, and filing date.
- ☐ Foreign priority will appear on the Filing Receipt in the following order: **Country, Application number, Filing date.**
- ☐ This application is the result of a conversion from a provisional application. Priority based on such application cannot be made since it no longer exists as a provisional application.

☒ The application(s) to which priority is claimed were filed over a year prior to the filing date of this application. Therefore, the referenced application(s) cannot be claimed as domestic or foreign priority.
60404137 and 60404145

☐ To change the benefit claim of a U.S. prior-filed application, applicant must amend the first sentence of the specification (if the benefit claim is referenced in the specification), or provide a supplemental application data sheet (ADS) (if the benefit claim was submitted in an ADS), with the desired benefit claim. Note that once a benefit claim is deleted, applicant will not be able to claim such prior-filed application again, if the above-identified application was filed on or after November 29, 2000.

☐ To change a foreign priority claim, applicant must submit a supplemental oath or declaration (if the priority claim is referenced in the oath or declaration), or a supplemental application data sheet (ADS) (if the priority claim was submitted in an ADS), with the desired priority claim. If a supplemental ADS is submitted, any deletions should be shown with strikeouts. Note that once a priority claim is deleted, applicant will not be able to claim such foreign application again, if the above-identified application was filed on or after November 29, 2000.

Customer Service Center
Initial Patent Examination Division (703) 308-1202

PART 1 - ATTORNEY/APPLICANT COPY

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March 6, 2007

VIA E-MAIL
CONFIRMATION VIA AIRMAIL

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Israel

Re:	U.S.S.N.:	10/767,064
	Title:	"Ex-Vivo Expansion of Hematopoietic Stem Cell Populations in Mononuclear Cell Cultures"
	Inventors:	Peled, *et al.*
	Filing Date:	January 29, 2004
	Our Ref.:	24024-506 CON
	Your Ref.:	GE:26736

Dear Gal:

Enclosed for your files is a copy of a Communication and related papers filed today in the U.S. Patent and Trademark Office for the above application.

If you have any questions, please do not hesitate to call us.

Sincerely,

Daniel W. Clarke

DWC/pjb
Enclosures
cc: Ivor R. Elrifi, Ph.D., Esq. (w/o enc)
Matthew Pavao, Ph.D., Esq. (w/o enc.)

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